Public Statement:

Cystatin C is a biomarker for inflammatory disease, especially kidney disease. Measuring this marker has not been shown to lead to improved outcomes, and this test is not covered.

Medical Policy Statement:

The measurement of Cystatin C for any indication is considered not medically necessary and is not covered.

Background:

There is no consensus in medical literature about the measurement of cystatin C or its true value in a number of medical conditions for which testing has been done. The use of this test has not been proven to improve outcomes and its higher cost is not justified.

Herget-Rosenthal et al reported a lack of creatinine reference methods and of calibration material though s-creatinine formulae provide accurate GFR estimates from 20-60 ml/min/1.73 m(2). S-cystatin C is sensitive to detect mild GFR reduction between 60 and 90 ml/min/1.73 m(2) but no reference method and no uniform calibration material exist for cystatin C either. Thyroid dysfunction, high glucocorticoid doses and potentially the presence of cardiovascular diseases can affect cystatin C levels. Cystatin C equations to estimate GFR have been proposed but this issue requires further evaluation.

Tidman et al presented validation of currently used formulae for eGFR based upon s-creatinine and s-cystatin C in 644 patients. Three creatinine-based equations (Cockcroft-Gault, MDRD, Jelliffe) and seven cystatin C based (Larsson, Hock, Filler, LeBrimon, Grubb, Orebro-cyst DAKO) were evaluated. Overall patients were correctly classified for the different stages of CKD in 62.1-64% for the creatinine based equations...
and 61.5-72% for the cystatin C based equations. They concluded estimating GFR using formulae based on s-creatinine or s-cystatin C alone was equally accurate according to the NKF K/DOQI guidelines.

Melander and associates published results of a study to evaluate biomarkers for predicting cardiovascular risks (Melander et al, 2009). Biomarkers studied included the older ones (CRP and N-BNP) as well as some of the newer ones including cystatin C, Lp-PLA2, MR-proADM and MR-proANP. Coronary and cardiovascular events, total mortality and total cardiovascular events were analyzed in this study of 5067 participants without cardiovascular disease with a median follow-up time of 12.8 years. According to the authors, “The best combinations of biomarkers were CRP and N-BNP for predicting cardiovascular events and MR-proADM and N-BNP for predicting coronary events. The use of multiple biomarkers minimally improve the accuracy of risk prediction models over and above conventional cardiovascular risk factors and did not reclassify a substantial proportion of individuals to higher or lower risk categories.”

This same study was discussed in an editorial by Shah and Lemos (Shah, 2009). In this editorial the authors stated that, “the investigators found that 5 of 6 biomarkers studied were independently associated with coronary and cardiovascular events, yet these associations were quantitatively modest (adjusted hazard ratio, 1.12-1.37 per standard deviation increment) and failed to substantially improve model discrimination or risk reclassification beyond traditional demographics and risk factors.”

The National Academy of Clinical Biochemistry released guidelines for the use of biomarkers for the prevention of cardiovascular disease and stroke (Myers, 2009). The guidelines included the following recommendations for the measurement of cystatin C as a predictor of cardiovascular events:

- Cystatin C may be a more powerful predictor of cardiovascular events than estimated GFR calculation based on creatinine. Research should be conducted to examine if interventions based on cystatin C measurements for risk stratification in individuals with diminished estimated GFR will provide added clinical benefit. (Classification of recommendation: Ila, Level of evidence: C)
- Properly designed studies focusing on the role of kidney disease markers (microalbumin, creatinine, estimated GFR, and cystatin C) should be conducted to characterize the utility of these markers in the global assessment of CVD risk in the primary prevention setting. (Classification of recommendation: I, Level of evidence: C)

References:


**Application to Products**

This policy applies to ARBenefits. Consult ARBenefits Summary Plan Description (SPD) for additional information.

Last modified by:  Date: